WHAT IS CLAIMED IS:

1. An isolated soluble non-fibrillar amyloid β oligomeric structure comprising from about 3 to about 24 amyloid β proteins that does not contain an exogenous added crosslinking agent and which exhibits neurotoxic activity.

2. An isolated oligomeric structure according to claim 1 wherein said oligomeric structure comprises trimer, tetramer, pentamer, hexamer, heptamer, octamer, 12-mer, 16-mer, 20-mer, or 24-mer aggregates of amyloid β proteins.

3. An isolated oligomeric structure according to claim 1 wherein said oligomeric structure has a molecular weight of from about 36 kD to about 108 kD as determined by non-denaturing gel electrophoresis.

4. An isolated oligomeric structure according to claim 1 wherein said oligomeric structure has a molecular weight of from about 26 kD to about 28 kD as determined by non-denaturing gel electrophoresis.

5. An isolated oligomeric structure according to claim 1 wherein said oligomeric structure has a molecular weight of from about 22 kD to about 24 kD as determined by electrophoresis on a 15% SDS-polyacrylamide gel.

6. An isolated oligomeric structure according to claim 1 wherein said oligomeric structure has a molecular weight of from about 18 kD to about 19 kD as determined by electrophoresis on a 15% SDS-polyacrylamide gel.

7 An isolated oligomeric structure according claim 1 wherein said oligomeric structure comprises globules of dimensions of from about 4.7 nm to about 11.0 nm as measured by atomic force microscopy.

8. An isolated oligomeric structure according claim 1 wherein said oligomeric structure comprises globules of dimensions of from about 4.7 nm to about 6.2 nm as measured by atomic force microscopy.

9. An isolated oligomeric structure according to claim 1 wherein said oligomeric structure comprises globules of dimensions of from about 4.9 nm to about 5.4 nm as measured by atomic force microscopy.

10. An isolated oligomeric structure according to claim 1 wherein said oligomeric structure comprises globules of dimensions of from about 5.7 nm to about 6.2 nm as measured by atomic force microscopy.

11. An isolated oligomeric structure according to claim 1 wherein said oligomeric structure comprises globules of dimensions of from about 6.5 nm to about 11.0 nm as measured by atomic force microscopy.

12. An isolated oligomeric structure according to claim 1 wherein from about 40% to about 75% of said oligomeric structure comprises globules of dimensions of from about 4.9 nm to about 5.4 nm, and dimensions of from about 5.7 nm to about 6.2 nm, as measured by atomic force microscopy.

13. An isolated oligomeric structure according to claim 1 wherein said oligomeric structure has a molecular weight of from about 13 kD to about 116 kD as determined by electrophoresis on a 16.5% tris-tricine SDS-polyacrylamide gel.

14. An isolated oligomeric structure according to claim 1 wherein said oligomeric structure has, as determined by electrophoresis on a 16.5% tris-tricine SDS-polyacrylamide gel, a molecular weight selected from the group consisting of from about 13 kD to about 14 kD, from about 17 kD to about 19 kD, from about 22 kD to about 23 kD, from about 26 kD to about 28 kD, from about 32 kD to about 33 kD, and from about 36 kD to about 38 kD.

15. A method for assaying the effects of an oligomeric structure according to claim 1 comprising:

(a) administering said oligomeric structure to the hippocampus of an animal;

(b) applying an electrical stimulus; and

(c) measuring the cell body spike amplitude over time to determine the long-term potentiation response.

16. The method of claim 15, wherein the long-term potentiation response of said animal is compared to the long-term potentiation response of another animal treated in the same fashion except having saline administered instead of oligomeric structure prior to application of said electrical stimulus.

17. A method for protecting an animal against decreases in learning or memory due to the effects of a soluble non-fibrillar amyloid ß oligomeric structure

according to claim 1, said method comprising administering a compound that blocks the formation or activity of said oligomeric structure.

18. A method for reversing in an animal decreases in learning or memory due to the effects of a soluble non-fibrillar amyloid ß oligomeric structure according to claim 1, said method comprising administering a compound that blocks the formation or activity of said oligomeric structure.

19. A method for protecting a nerve cell against decreases in long-term potentiation due to the effects of a soluble non-fibrillar amyloid ß oligomeric structure according to claim 1, said method comprising contacting said cell with a compound that blocks the formation or activity of said oligomeric structure.

20. A method for reversing in a nerve cell decreases in long-term potentiation due to the effects of a soluble non-fibrillar amyloid ß oligomeric structure according to claim 1, said method comprising contacting said cell with a compound that blocks the formation or activity of said oligomeric structure.

21. A method for protecting a nerve cell against aberrant neuronal signaling due to the effects of a soluble non-fibrillar amyloid ß oligomeric structure according to claim 1, said method comprising contacting said cell with a compound that blocks the formation or activity of said oligomeric structure.

22. A method for detecting in a test material the oligomeric structure according to claim 1 comprising:

(a) contacting said test material with 6E10 antibody; and

(b) detecting binding to said oligomeric structure of said antibody.

23. A method for detecting in a test material the oligomeric structure according to claim 1 comprising:

(a) contacting said test material with serum-starved neuroblastoma cells; and

(b) measuring morphological changes in said cells by comparing the morphology of said cells against neuroblastoma cells that have not been contacted with said test material.

24. A method for detecting in a test material the oligomeric structure according to claim 1 comprising:

(a) contacting said test material with brain slice cultures; and

(b) measuring brain cell death as compared against brain slice cultures that have not been contacted with said test material.

25. A method for detecting in a test material the oligomeric structure according to claim 1 comprising:

(a) contacting said test material with neuroblastoma cells; and

(b) measuring increases in Fyn kinase activity by comparing Fyn kinase activity in said cells against Fyn kinase activity in neuroblastoma cells that have not been contacted with said test material.

26. A method for detecting in a test material the oligomeric structure according to claim 1 comprising:

(a) contacting said test material with cultures of primary astrocytes; and

(b) determining activation of said astrocytes as compared to cultures of primary astrocytes that have not been contacted with said test material.

27. A method for detecting in a test material the oligomeric structure according to claim 1 comprising:

(a) contacting said test material with cultures of primary astrocytes; and

(b) measuring in said astrocytes increases in the mRNA for proteins selected from the group consisting of interleukin-1, inducible nitric oxide synthase, Apo E, Apo J, and α1-antichymotrypsin by comparing said mRNA levels in said astrocytes against the corresponding mRNA levels in cultures of primary astrocytes that have not been contacted with said test material.

28. A method for identifying compounds that modulate the effects of an oligomeric structure according to claim 1 comprising:

(a) administering either saline or a test compound to the hippocampus of an animal;

(b) applying an electrical stimulus;

(c) measuring the cell body spike amplitude over time to determine the long-term potentiation response; and

(d) comparing the long-term potentiation response of animals having saline administered to the long-term potentiation response of animals having test compound administered

with the proviso that administration of said oligomeric structure is not done for therapy.

29. The method of claim 28 which further comprises administering oligomeric structure to said hippocampus either before, along with, or after administering said saline or test compound.

30. A method for identifying compounds that block the neurotoxicity of the oligomeric structure according to claim 1 comprising:

(a) contacting separate cultures of neuronal cells with said oligomeric structure either in the presence or absence of contacting with said test compound;

(b) measuring the proportion of viable cells in each culture; and

(c) comparing the proportion of viable cells in each culture, with compounds that block the neurotoxicity of said oligomeric structure being identified as resulting in an increased proportion of viable cells in said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound.

31. A method for identifying compounds that block binding to a cell surface protein of the oligomeric structure according to claim 1 comprising:

(a) contacting separate cultures of neuronal cells with said oligomeric structure either in the presence or absence of contacting with said test compound;

(b) adding a reagent that binds to said oligomeric structure, said reagent being fluorescent;

(c) analyzing said separate cell cultures by fluorescence-activated cell sorting; and

(d) comparing the fluorescence of the cultures, with compounds that block binding to a cell surface protein of the oligomeric structure being identified as resulting in a reduced fluorescence of said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound.

32. A method for identifying compounds that block binding to a cell surface protein of the oligomeric structure according to claim 1 comprising:

(a) forming said oligomeric structure from amyloid β protein such that it becomes a labeled oligomeric structure comprising a binding moiety capable of binding a fluorescent reagent;

(b) contacting separate cultures of neuronal cells with said labeled oligomeric structure either in the presence or absence of contacting with said test compound;

(c) adding a fluorescent reagent that binds to said oligomeric structure;

(d) analyzing said separate cell cultures by fluorescence-activated cell sorting; and

(e) comparing the fluorescence of the cultures, with compounds that block binding to a cell surface protein of the oligomeric structure being identified as resulting in a reduced fluorescence of said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound.

33. A method for identifying compounds that block formation or binding to a cell surface protein of the oligomeric structure according to claim 1 comprising:

(a) preparing separate samples of amyloid β protein that either have or have not been mixed with said test compound;

(b) forming said oligomeric structure in said separate samples;

(c) contacting separate cultures of neuronal cells with said separate samples;

(d) adding a reagent that binds to said oligomeric structure, said reagent being fluorescent;

(e) analyzing said separate cell cultures by fluorescence-activated cell sorting; and

(f) comparing the fluorescence of the cultures, with compounds that block formation or binding to a cell surface protein of the oligomeric structure being identified as resulting in a reduced fluorescence of said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound.

34. A method for identifying compounds that block formation or binding to a cell surface protein of the oligomeric structure according to claim 1 comprising:

(a) preparing separate samples of amyloid β protein that either have or have not been mixed with said test compound;

(b) forming said oligomeric structure in said separate samples such that it becomes a labeled oligomeric structure comprising a binding moiety capable of binding a fluorescent reagent in each of said separate samples;

(c) contacting separate cultures of neuronal cells with said separate samples;

(d) adding a fluorescent reagent that binds to said oligomeric structure;

(e) analyzing said separate cell cultures by fluorescence-activated cell sorting; and

(f) comparing the fluorescence of the cultures, with compounds that block formation or binding to a cell surface protein of the oligomeric structure being identified as resulting in a reduced fluorescence of said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound.

35. The method of claim 33, wherein the fluorescence of said cultures further is compared with the fluorescence of cultures that have been treated in the same fashion except that instead of adding or not adding test compound prior to formation of the oligomeric structure, said test compound either is or is not added after formation of the oligomeric structure,

with compounds that block formation of the oligomeric structure being identified as resulting in a reduced fluorescence of said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound, only when said compound is added prior to oligomeric structure, and

compounds that block binding to a cell surface protein of the oligomeric structure being identified as resulting in a reduced fluorescence of said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound, when said compound is added either prior to or after oligomeric structure.

36. The method of claim 33, wherein the fluorescence of said cultures further is compared with the fluorescence of cultures that have been treated in the same fashion except that instead of adding or not adding test compound prior to formation of the oligomeric structure, said test compound either is or is not added after formation of the oligomeric structure,

with compounds that block formation of the oligomeric structure being identified as resulting in a reduced fluorescence of said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound, only when said compound is added prior to oligomeric structure, and

compounds that block binding to a cell surface protein of the oligomeric structure being identified as resulting in a reduced fluorescence of said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound, when said compound is added either prior to or after oligomeric structure.

37. A method of detecting binding to a cell surface protein of the oligomeric structure according to claim 1 comprising:

(a) forming said oligomeric structure from amyloid β protein;

(b) contacting a culture of neuronal cells with said oligomeric structure;

(c) adding an antibody that binds said oligomeric structure, said antibody including a conjugating moiety;

(e) washing away unbound antibody;

(f) linking an enzyme to said antibody bound to said oligomeric structure by means of said conjugating moiety;

(g) adding a colorless substrate that is cleaved by said enzyme to yield a color change; and

(h) determining said color change as a measure of binding to a cell surface protein of said oligomeric structure.

38. A method for identifying compounds that block binding to a cell surface protein of the oligomeric structure according to claim 1 comprising:

(a) preparing separate samples of amyloid β protein that either have or have not been mixed with said test compound;

(b) forming said oligomeric structure in said separate samples;

(c) contacting separate cultures of neuronal cells with said separate samples;

(d) adding an antibody that binds said oligomeric structure, said antibody including a conjugating moiety;

(e) washing away unbound antibody;

(f) linking an enzyme to said antibody bound to said oligomeric structure by means of said conjugating moiety;

(g) adding a colorless substrate that is cleaved by said enzyme to yield a color change; and

(h) comparing the color change produced by each of said separate samples, with compounds that block formation or binding to a cell surface protein of the

oligomeric structure being identified as resulting in a reduced color change produced by said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound.

39. The method of claim 38, wherein the color change produced by said cultures further is compared with the color change produced by cultures that have been treated in the same fashion except that instead of adding or not adding test compound prior to formation of the oligomeric structure, said test compound either is or is not added after formation of the oligomeric structure,

with compounds that block formation of the oligomeric structure being identified as resulting in a reduced color change produced by said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound, only when said compound is added prior to oligomeric structure, and compounds that block receptor binding of the oligomeric structure being identified as resulting in a reduced color change produced by said culture as compared to the corresponding culture contacted with said oligomeric structure in the absence of said test compound, when said compound is added either prior to or after oligomeric structure.

40. A method for identifying compounds that block formation of the oligomeric structure according to claim 1 comprising:

(a) preparing separate samples of amyloid β protein that either have or have not been mixed with said test compound;

(b) forming said oligomeric structure in said separate samples;

(c) assessing whether any protein assemblies have formed in the separate samples using a method selected from the group consisting of electrophoresis, immunorecognition, and atomic force microscopy; and

(d) comparing the formation of said protein assemblies in said separate samples, which compounds that block formation of said oligomeric structure being identified as resulting in decreased formation of said oligomeric structure in said sample as compared with a sample in which said oligomeric structure is formed in the absence of said test compound.

41. A method of preparing an isolated soluble, globular, non-fibrillar amyloid β oligomeric structure according to claim 1, wherein said method comprises:

(a) obtaining a solution of monomeric amyloid β protein, said amyloid β protein being capable of forming said oligomeric structure;

(b) diluting said protein solution into an appropriate media to a final concentration of from about 5 nM to about 500 μM;

(c) incubating the media resulting from step (b) at about 4°C for from about 2 hours to about 48 hours;

(c) centrifuging said solution at about 14,000 g at about 4°C; and

(d) recovering the supernatant resulting from said centrifugation as containing said amyloid β oligomeric structure.

42. The method of claim 41, wherein said method comprises incubating the media resulting from step (b) at about 4°C in the presence of clusterin.

43. A method for preparing a soluble non-fibrillar amyloid ß oligomeric structure according to claim 1, wherein said method comprises:

(a) obtaining a solution of monomeric amyloid β protein, said amyloid β protein being capable of forming said oligomeric structure;

(b) dissolving said amyloid β monomer in hexafluoroisoproanol;

(c) removing hexafluoroisoproanol by speed vacuum evaporation to obtain solid peptide;

(d) dissolving said solid peptide in DMSO to form a DMSO stock solution;

(e) diluting said stock solution into an appropriate media;

(f) vortexing; and

(g) incubating at about 4°C for about 24 hours.

44. A method for detecting in a test material the oligomeric structure according to claim 1 comprising:

(a) contacting said test material with a nerve cell; and

determining whether said cell exhibits ADDL-induced aberrant neuronal signaling.